HOW DO NEURONS DEGENERATE IN TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES

P.P.Liberski, EM Lab, Chair Oncol., Med. Academy Lodz, Lodz, Poland

While the mechanisms by which neurons degenerate in subacute spongiform encephalopathies are largely unknown, two basic processes are recognized: neuroaxonal dystrophy (NAD) and formation of autophagic vacuoles (AV). AV were observed in both experimental CJD in mice and scrapie but they were more abundant in the latter. AV were observed only in neuronal perikarya and their processes but not glial cells. AV consisted of areas of the cytoplasm being sequestrated with single, double or multiple membranes. Sequestrated cytoplasm contained ribosomes, occasionally mitochondria, small secondary vacuoles with vesicles, or presented homogenously dense appearance, presumably reflecting degenerative changes. The pathomechanism by of which NAD develops is yet to be elucidated, but the disturbances of both anterograde and retrograde axoplasmic flow contribute to the formation of dustrophic neurites (DN). By immunohistochemistry with anti-200 kDa neurofilamet protein (NFP) antibodies, neuritic distensions were observed mainly in the white matter, but also at the junction between gray and white matter. They were ovoid or elongated in shape. Most were connected to one end of an axon but many appeared as bullous swellings along the course of axon. In several axons, 3 or 4 such distensions could be traced along the visible part of the axonal segment. Noteworthy, such immunostained neurites adapted to other pre-existing structures as vessels and, particularly, spongiform vacuoles. In such locations they were distorted and bent. Still other distensions clearly encompassed typical CJD vacuoles. In such situations vacuoles were surrounded by a narrow ring of strong immunopositivity. Furthermore, several neurons were observed with vacuoles distending immunopositive branching dendrites. The smaller blebs and globules were frequently seen and these probably corresponded to DN of smaller diameters cut in transverse planes. Larger spheroids were observed mostly within medulla predominantly but not exclusively in anterior horns. They were larger than neuritic swellings and strongly immunopositive for NFP. Immunopositivity, sometimes located at the periphery, was of diffuse or granular type and small vacuoles were frequently seen within larger spheroids. Larger spheroids, in turn, were often surrounded by smaller ones or by clusters of immunopositive blebs and globules.

Supported by the KBN grant and a part of EC Biomed-1 project "Prion disorders"

Source: https://www.industrydocuments.ucsf.edu/docs/hzdb0000